APPENDIX A:

Pending Claims Showing Amendments after Response to Office Action dated 10/24/00

1. (Amended three times) A method of identifying a candidate substance that inhibits the aggregation of a mammalian aggregate-prone amyloid protein, comprising:

(a) contacting a yeast cell that expresses a chimeric [an] aggregate-prone amyloid protein comprising a mammalian aggregate-prone amyloid peptide with said candidate substance under conditions effective to allow aggregated amyloid formation; and

(b) determining the ability of said candidate substance to inhibit the aggregation of the aggregate-prone amyloid protein.

3. The method of claim 1, wherein the mammalian aggregate-prone amyloid protein comprises a PrP or β-amyloid polypeptide.

4. [Cancelled]

7. (Amended twice) The method of claim 1 [4], wherein the chimeric protein comprises at least an aggregate forming domain of a mammalian aggregate-prone amyloid protein operably attached to a detectable marker protein.

8. The method of claim 7, wherein said marker protein is green fluorescent protein or luciferase.

9. The method of claim 7, wherein said marker protein is a drug-resistance marker protein.

10. The method of claim 7, wherein said marker protein is a hormone receptor.

11. The method of claim 10, wherein said hormone receptor is a glucocorticoid receptor.

12. (Amended twice) The method of claim 1 [4], wherein the chimeric protein comprises at least an aggregate forming domain of PrP or β-amyloid.

13. The method of claim 12, wherein the chimeric protein comprises as least about amino acids 1-42 of β-amyloid protein.

14. (Amended twice) The method of claim 1 [4], wherein the chimeric protein comprises Sup35 in which the N-terminal domain has been replaced by amino acids 1-42 of β-amyloid protein.

15. The method of claim 1, wherein any aggregation of the mammalian aggregate-prone amyloid protein is detected by the ability of the aggregated protein to bind Congo Red.

16. The method of claim 1, wherein any aggregation of the mammalian aggregate-prone amyloid protein is detected by increased protease resistance of the aggregated protein.

17. The method of claim 1, wherein the aggregate-prone amyloid protein is labeled.

18. The method of claim 17, wherein the label is a radioactive isotope, a fluorophore, or a chromophore.

19. The method of claim 18, wherein the label is ^{35}S.

20. The method of claim 18, wherein the fluorophore comprises a green fluorescent protein polypeptide.

22. The method of claim 1, wherein said yeast cell overexpresses Hsp104.

37. The method of claim 1, wherein aggregated amyloid formation is evidenced by the formation of fibrillary material.

38. A method of identifying a candidate substance that inhibits mammalian aggregate-prone amyloid proteins from forming a fibril, comprising:

(a) contacting a yeast cell that expresses an aggregate-prone amyloid protein comprising a mammalian aggregate-prone amyloid protein with the candidate substance under conditions effective to allow fibril formation; and

(b) determining the ability of said candidate substance to inhibit the aggregate-prone amyloid protein from forming a fibril.

39. The method of claim 38, wherein the aggregate-prone amyloid protein comprises a PrP or β-amyloid polypeptide.

40. The method of claim 38, wherein the aggregate-prone amyloid protein is a chimeric protein.

APPENDIX B:

Claims Pending after Response to Office Action dated October 24, 2000

1. A method of identifying a candidate substance that inhibits the aggregation of a mammalian aggregate-prone amyloid protein, comprising:

(a) contacting a yeast cell that expresses a chimeric aggregate-prone amyloid protein comprising a mammalian aggregate-prone amyloid peptide with said candidate substance under conditions effective to allow aggregated amyloid formation; and

(b) determining the ability of said candidate substance to inhibit the aggregation of the aggregate-prone amyloid protein.

3. The method of claim 1, wherein the mammalian aggregate-prone amyloid protein comprises a PrP or β-amyloid polypeptide.

7. The method of claim 1, wherein the chimeric protein comprises at least an aggregate forming domain of a mammalian aggregate-prone amyloid protein operably attached to a detectable marker protein.

8. The method of claim 7, wherein said marker protein is green fluorescent protein or luciferase.

9. The method of claim 7, wherein said marker protein is a drug-resistance marker protein.

10. The method of claim 7, wherein said marker protein is a hormone receptor.

11. The method of claim 10, wherein said hormone receptor is a glucocorticoid receptor.

12. The method of claim 1, wherein the chimeric protein comprises at least an aggregate forming domain of PrP or β-amyloid.

13. The method of claim 12, wherein the chimeric protein comprises as least about amino acids 1-42 of β-amyloid protein.

14. The method of claim 1, wherein the chimeric protein comprises Sup35 in which the N-terminal domain has been replaced by amino acids 1-42 of β-amyloid protein.

15. The method of claim 1, wherein any aggregation of the mammalian aggregate-prone amyloid protein is detected by the ability of the aggregated protein to bind Congo Red.

16. The method of claim 1, wherein any aggregation of the mammalian aggregate-prone amyloid protein is detected by increased protease resistance of the aggregated protein.

17. The method of claim 1, wherein the aggregate-prone amyloid protein is labeled.

18. The method of claim 17, wherein the label is a radioactive isotope, a fluorophore, or a chromophore.

19. The method of claim 18, wherein the label is ^{35}S.

20. The method of claim 18, wherein the fluorophore comprises a green fluorescent protein polypeptide.

22. The method of claim 1, wherein said yeast cell overexpresses Hsp104.

37. The method of claim 1, wherein aggregated amyloid formation is evidenced by the formation of fibrillary material.

38. A method of identifying a candidate substance that inhibits mammalian aggregate-prone amyloid proteins from forming a fibril, comprising:

(a) contacting a yeast cell that expresses an aggregate-prone amyloid protein comprising a mammalian aggregate-prone amyloid protein with the candidate substance under conditions effective to allow fibril formation; and

(b) determining the ability of said candidate substance to inhibit the aggregate-prone amyloid protein from forming a fibril.

39. The method of claim 38, wherein the aggregate-prone amyloid protein comprises a PrP or β-amyloid polypeptide.

40. The method of claim 38, wherein the aggregate-prone amyloid protein is a chimeric protein.